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ORGANIC CHEMISTRY

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EXHIBIT

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To Our Parents and to Cathy

Organic Chemistry

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Deuterium Exchange and Halogenation Reactions of Carbonyl Derivatives

23.7 Mechanisms of α Epimerization, Bromination, and Deuterium Exchange of Ketones

In the presence of acidic or basic catalysts, carbonyl derivatives with α hydrogens react with halogens to give α -halo carbonyls. They undergo deuterium exchange in such solvents as D_2O or CH_3OD , and carbonyl derivatives with chiral α sites racemize. Let us examine evidence that implies that enols or enolate anions are intermediates in all these reactions.

In a series of papers published in 1936 to 1938, C. K. Ingold and co-workers reported that (*R*)-*sec*-butyl phenyl ketone racemizes slowly in aqueous solvents in the presence of acids or bases. If D_2O is used as a solvent, racemic α -deuterated ketone is observed. If the solvent contains bromine, a racemic mixture of α -bromo ketones is formed. All these results are summarized in Figure 23.6.

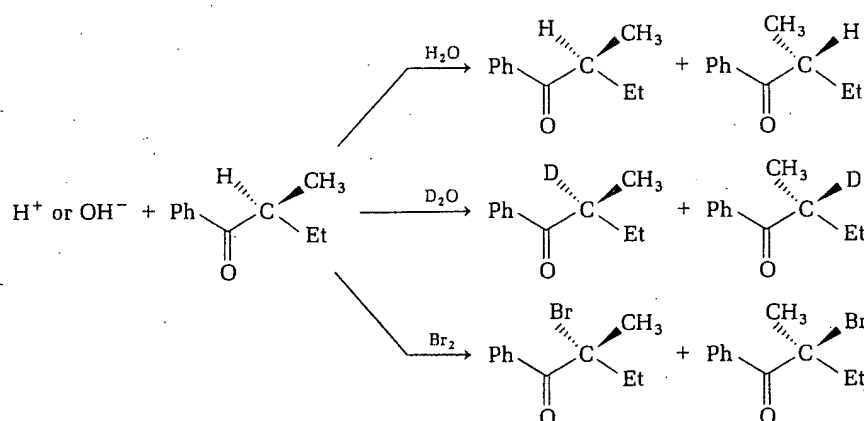


Figure 23.6
Acid- and base-catalyzed transformations of *sec*-butyl phenyl ketone.

Two striking facts are apparent if the rates of these reactions are measured:

1. The racemization, bromination, and deuterium exchange reactions take place at the same rate.
2. The rate law for bromination is first order in ketone concentration and first order in catalyst concentration but independent of bromine concentration.

$$\text{Rate of formation of bromoketone} = k[\text{ketone}][\text{catalyst}]$$

We conclude that the rate-determining transition state for bromination contains the catalyst and the ketone but cannot contain a bromine molecule. The reaction mechanism must therefore involve an intermediate that reacts with

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bromine rapidly, after the rate-determining step. Moreover, that intermediate is achiral, since the rates of racemization and bromination are identical and only racemic bromide is formed.

The reasonable intermediates we can propose for these reactions are the enol or the enolate ion. The rate-determining transition state for all three reactions involves transfer of an α hydrogen to a base, forming the enol or enolate. The product-forming transition states involve combination of the enol or enolate ion with bromine or D_2O ; these transition states are lower in energy, as shown in Figure 23.7. This mechanism is believed to hold generally for racemization, deuterium exchange, and halogenation at the sites α to carbonyl, cyano, and nitro groups. To predict the rates of these reactions we need only understand the rates of enol or enolate formation.

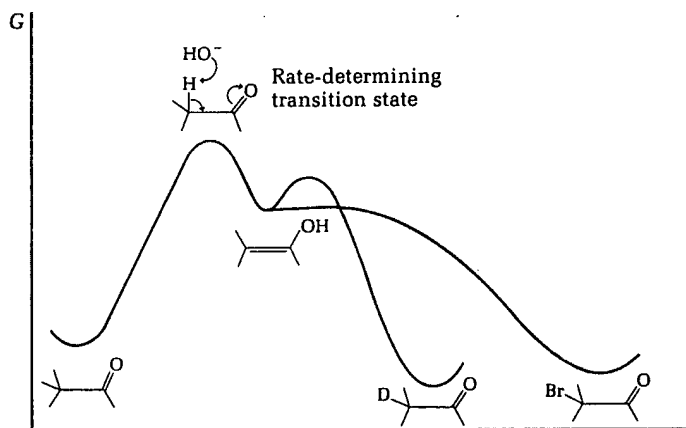
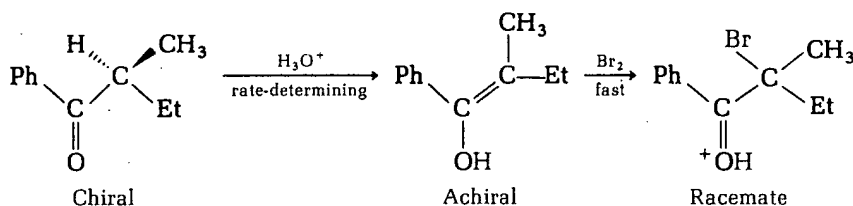


Figure 23.7
Energy diagram for α deuteration and bromination.

Problem 23-8 What would you expect the rate of bromination of hexadeuteroacetone to be, relative to acetone? Explain your answer.

Problem 23-9 Ketones also undergo an acid- and base-catalyzed oxygen-exchange reaction with $^{18}\text{OH}_2$. Give a mechanism for this reaction. If $^{18}\text{OD}_2$ were used, would you expect the rate of oxygen exchange to be the same as the rate of deuterium exchange? Why or why not?

Problem 23-10 Knowing that the conversion of keto into enol tautomer is slower than the rate of bromination of the enol, how would you determine the equilibrium percentage of enol tautomer in a keto-enol mixture?

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